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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,071	02/13/2002	David Bar-Or	4172-3-2	8825

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EXAMINER

DESAI, ANAND U

ART UNIT PAPER NUMBER

1653

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/076,071		BAR-OR ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Anand U. Desai, Ph.D.		1653	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 December 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 531-576 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 531-576 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>20050309</u> .  | 6) <input type="checkbox"/> Other: _____                                    |

*A*

### **DETAILED ACTION**

1. This office action is in response to Amendment filed on December 22, 2004. Claims 1-530 have been cancelled. New claims 574-576 have been added. Claims 531-576 are currently pending and are under examination.

#### **Withdrawal of Rejections**

2. The provisional rejection of claims 531-573 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 83-118 of copending Application No. 10/186,168 is withdrawn based on Applicants cancellation of claims 83-118 in copending Application.

3. The rejection of claims 542, 556, 557, 559-562, and 569-573 under 35 U.S.C. 112, 2<sup>nd</sup> paragraph is withdrawn based on Applicant's amendment to the claims.

4. The rejection of claims 531-573 under 35 U.S.C. 103(a) as being unpatentable over Blaschuk et al. (U.S. Patent 6,610,821 B1) in view of Sijmons et al. (U.S. Patent 5,650,307) is withdrawn based on Applicant's amendment to the claims.

#### **Maintenance of Objections and Rejections**

##### ***Specification***

5. The disclosure is objected to because of the following informalities:

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The hyperlink is located on page 15, line 20.

Appropriate correction is required.

*Claim Objections*

7. Claim 532 is objected to because of the following informalities: the status identifier should be (Previously presented) as opposed to (New). Appropriate correction is required.

*Claim Rejections - 35 USC § 112*

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 561, 562, and 569-576 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. In claim 561, the formula with a substituent (R<sub>3</sub>)<sub>2</sub> on the α-amino group is contrary to the limitation in claim 531 (see page 10 of 21 of amendment dated December 22, 2004, figure on top right hand side)? Clarification is required. Claims 562, and 569-576 are rejected for depending on rejected claim 561.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 531-576 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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13. Applicant's amendment asserts that no New Matter has been added and points to the specification at pages 7, line 10 through page 8, line 8, page 14, line 25 through page 16, line 5, page 19, line 14 through page 20, line 11, page 37, lines 17-25, and examples 1, and 8-10 of the application, for support for the newly added limitation "Xaa1 has an unsubstituted  $\alpha$ -amino group". However, the specification does not appear to provide an adequate written description of "Xaa1 has an unsubstituted  $\alpha$ -amino group". The cited sections of the specification disclose the general formula of the peptide, P1-P2, where P1 and P2 are further defined, methods for making the peptide that are well known in the art, the use of metal-binding compounds of the invention to treat a variety of diseases and conditions, and the synthesis/use of a tetrapeptide Asp-Ala-His-Lys in the inhibition of reactive oxygen species. The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112. *Applicant is required to cancel the New Matter in the response to this Office Action.* Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

MPEP 2163.06 notes, "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." The introduction of claim changes, which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d

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1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species).

***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 531-576 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al. (Neurosurgery 37(2): 287-293 (1995)) in view of Harford and Sarkar (Acc. Chem. Res. 30: 123-130 (1997)). Yoshida et al. discloses the effects of copper chelation on angiogenesis. Yoshida et al. analyzed tumor weight, and vascular density of rats feed with a copper depletion diet and treated with a copper chelator, D-penicillamine. Yoshida et al. show by histological findings that treated rats have a significantly smaller vascular density compared to a control group of rats (see pp. 289-290, Section on Vascular density and pathological study, Figures 3,

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and 4). Yoshida et al. demonstrates the inhibition of angiogenesis achieved by chelating copper (see Introduction, pp.287). Yoshida et al. does not disclose the use of the peptide having the formula claimed.

Harford and Sarkar disclose the amino terminal copper and nickel-binding motif found in proteins (see Introduction, pp.123). Harford and Sarkar disclose the binding of copper and nickel to the amino acid sequence Asp-Ala-His, which is the peptide being claimed by the formula in claim 531 (see Figure 3-5, pp. 125). Harford and Sarkar describe the importance of the Histidine residue being in the 3<sup>rd</sup> position of an amino acid sequence to bind a copper ion (see section on Design of the ATCUN Motif, pp. 126). Harford and Sarkar further disclose the synthetic design of a metal binding site onto a protein, to produce a hybrid protein that is currently being claimed (see Protein Design Utilizing the ATCUN Motif pp. 128, and Conclusion, pp. 130, see current application, claim 531, 542, and 550 in particular).

One would have been motivated to design a metal binding peptide as described in Harford and Sarkar, to chelate copper ions and inhibit angiogenesis as disclosed by Yoshida et al. to treat various angiogenic diseases or conditions, including neoplasms. Therefore, it would have been obvious to a person having ordinary skill in the art to administer a metal binding peptide to treat an angiogenic disease or condition (current application, claims 531-576).

#### Response to Remarks

Applicants traverse this rejection. Applicants state that Harford and Sarkar describe a copper-binding motif found in certain proteins. The motif is referred to as the ATCUN motif, and the structural characteristics of this motif are described in Harford and Sarkar. Applicants further state that however, Harford and Sarkar also report that the ATCUN motif can also release

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the metal easily with appropriate ligands, reflecting its role as a transport site in albumins (see e.g., Introduction). Applicants state the peptide of the present invention comprises an ATCUN motif. Applicants state that Yoshida et al. describes a study of the effects of a combination of a copper-depletion diet and D-penicillamine (a copper chelator) on tumor growth and angiogenesis in a rat model (citing Abstract, and Materials and Methods sections). The decrease in tumor growth was attributed to the suppression of angiogenesis by the CDPT (see Abstract). The copper chelator investigated by Yoshida et al. was D-penicillamine. Applicant quotes a sentence in Yoshida's discussion to suggest that not all copper chelators would be expected to inhibit angiogenesis; "More research and complex calculations relating to affinity and transfer kinetics are required to determine whether a carrier molecule becomes a stimulator of cell growth by delivering Cu or whether it becomes an inhibitor of cell growth by removing the bioactivity of the Cu ion." Applicant's state that Yoshida et al. is an invitation to experiment to determine additional copper chelators that would be effective in inhibiting angiogenesis. Applicant contends that based on the combined teachings of Yoshida et al. and Harford and Sarkar, those skilled in the art would not have expected the peptides employing the ATCUN motif to inhibit angiogenesis or could be used to treat angiogenic diseases and conditions. Therefore would not have made the claimed invention obvious. This is not found persuasive. Harford and Sarkar do disclose the synthetic design of a metal binding site onto a protein, to produce a hybrid protein that is currently being claimed (see Protein Design Utilizing the ATCUN Motif, pp. 128 and Conclusion, pp. 130). Therefore, one would have been motivated to design a metal binding peptide as described in Harford and Sarkar, to chelate copper ions and inhibit angiogenesis as disclosed by Yoshida et al. to treat various angiogenic diseases or conditions (see Introduction,



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and last sentence of 4<sup>th</sup> paragraph of Conclusion section titled Copper chelation and angiogenesis).

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 7:00 a.m. - 3:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 26, 2005



KAREN COCHRANE CARLSON, PH.D.  
PRIMARY EXAMINER